Chinese Journal of Chemistry 2006 24 (10): 1279-1281 ISSN: 0567-7351 CN: 31-1320/06

Communications

组氨酸残基在芳基胺类**N**-乙酰基转移酶（**NATs**）乙酰化过程中有何作用？--量子化学研究

乔青安[1*],蔡政亭[2],杨传路[3],王美山[3]

[a]烟台师范学院化学与材料科学学院，烟台264025, 中国
[b]山东大学理论化学研究所, 济南 250100, 中国
[c]烟台师范学院物理系，烟台264025, 中国

收稿日期 2006-1-26 修回日期 2006-6-26 网络版发布日期 2006-12-14 接受日期

摘要 芳基胺类N-乙酰基转移酶能够催化辅酶A与芳基胺的乙酰基转移反应，对药物、致癌物的代谢及生物活化有重要意义。实验认为组氨酸残基（His-107）可能参与乙酰基转移反应。本文用密度泛函方法研究了乙酰化过程的详细机理，结果表明：当乙酰基直接从给体转移到受体时，活化势垒很高，反应难以进行；当His-107参与反应时，活化能稍有降低（20-25

kJ/mol）；而当His-107质子化后再参与反应时，活化能大幅降低 （73-85 kJ/mol），乙酰化反应极易完成，且该过程经历一个硫醇-咪唑盐式中间体。计算结果证实了实验推测。

关键词 芳基胺类N-乙酰基转移酶 2,密度泛函理论,乙酰基转移,组氨酸残基（His-107）
分类号

What a Role did Histidine Residue Play in Arylamine *N*-Acetyltransferase 2 Acetylation? A Quantum Chemistry Study

QIAO Qing-An*,[a], CAI Zheng-Ting[b], YANG Chuan-Lu[c], WANG Mei-Shan[c]

[a] *School of Chemistry and Materials Science, Yantai Normal University, Yantai, Shandong 264025, China*
[b] *Institute of Theoretical Chemistry, Shandong University, Jinan, Shandong 250100, China*
[c] *Department of Physics, Yantai Normal University, Yantai, Shandong 264025, China*

Abstract Arylamine *N*-acetyltransferases (NATs, EC 2.3.1.5) catalyze an acetyl group transfer from acetyl coenzyme A (AcCoA) to primary arylamines and play a very important role in the metabolism and bioactivation of drugs and carcinogens. Experiments revealed that His-107 was likely the residues responsible for mediating acetyl transfer. The full catalytic mechanism of acetylation process has been examined by density functional theory. The results indicate that, if the acetyl group is directly transferred from the donor, *p*-nitrophenyl acetate, to the acceptor, cysteine, the high activation energy will be a great hindrance. These energies have dropped in a little range of 20—25 kJ/mol when His-107 assisted the transfer process. However, when protonated His-107 mediated the reaction, the activation energies have been dropped about 73—85 kJ/mol. Our calculations strongly supported an enzyme acetylation mechanism that experiences a thiolate-imidazolium pair, and verified the presumption from experiments.

Key words arylamine *N*-acetyltransferase 2 density functional theory acetyl transfer role of His-107

DOI:

通讯作者 乔青安 qiaoqa@hotmail.com or qiaoqa@sdu.edu.cn